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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/881,326 | 06/14/2001 | David B. Rozema | Mirus.013.02 | 1467 |

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| EXAMINER |
|---|
| SANDALS, WILLIAM O |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 08/14/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/881,326 | Rozema et al. |
| **Examiner** | **Art Unit** |
| William Sandals | 1636 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *Jun 14, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Jun 14, 2001* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Drawings*

1. The drawings as submitted on June 14 2001, have been approved by the draftsman.

### *Double Patenting*

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-19 of U.S. Patent No. 6,383,811 in view of US 5,698,531. Claims 13-19 of U.S. Patent No. 6,383,811 are drawn to a process of delivering a polynucleotide to a blood vessel and then to an extravascular cell. The polynucleotide is delivered in a complex comprising the polynucleotide and a cationic polymer (such as PEI) where the charge on the complex is less negative than the charge on the polynucleotide, then expressing the polynucleotide in the extravascular cell. Claims 1-3 of the instant claimed invention are drawn to a process of delivering a polynucleotide/polymer complex which has a zeta potential less negative than the polynucleotide to an extravascular parenchymal cell, increasing the permeability of the blood vessel and expressing the polynucleotide in the parenchymal cell. The polycation may have a pKa of 5-7 and the polymer may consist of imidazole groups, pyridine groups or aniline groups.

The instant specification states that PEI is a polymer which is well known in the prior art to have a pKa in the range of 5-7 at physiological pH. US 5,698,531 taught (see especially the abstract and columns 4-7) the obvious and desirable increasing of the permeability of a vessel to deliver a polynucleotide complex to the extravascular cells (parenchymal cells, as defined in the instant specification), making increasing the permeability of a vessel to deliver a polynucleotide complex to an extravascular parenchymal cell obvious .

4. Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of copending Application No. 09/447,966. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-5 of copending Application No. 09/447,966 are drawn to a process of delivering a polynucleotide to an extravascular parenchymal cell where the polynucleotide is in a complex with an amphipathic compound, inserting the complex into a blood vessel, increasing the permeability of the blood vessel to deliver the polynucleotide to an extravascular parenchymal cell and expressing the polynucleotide in the parenchymal cell. Claims 1-3 of the instant claimed invention are drawn to a process of delivering a polynucleotide in a complex with a polymer where the complex has a zeta potential less negative than the polynucleotide into a blood vessel, increasing the permeability of the blood vessel, delivering the complex to an extravascular parenchymal cell and expressing the polynucleotide in the parenchymal cell.

5. The instant specification states that PEI is a polymer known in the prior art which may be used in to form the instant claimed polymer complex, and further states that PEI is an ampholite which is known in the prior art to have a pKa in the range of 5-7 at physiological pH.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### *Claim Rejections - 35 USC § 112*

6.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites "the polymer selected from the group consisting of imidazole, pyridine, or aniline groups". The recitation of the "group" in the first instance is made unclear by the following recitation of "groups". The language may be interpreted to mean that the "group" (first instance) consists of all of the "groups" (second instance). If **all** (emphasis added) of the groups are intended to be part of the "group" (first instance), then there is no "group". If on the other hand, each of the members of the group is intended to be a selection which is distinct from each of the other members of the group, then a clarification of this issue is required to eliminate the indefiniteness of the claim. Adding "groups" after each of "imidazole" and "pyridine" would provide this distinction and clarify the intent of the claim. Further, it is not clear from the language if the polymer is to consist wholly of one of the members of the "group". As the claim is written the "group" or "groups" may not indeed be polymerized. Thus, the claim is vague and indefinite. For purposes of examination, it is assumed that the polymer is made up of repeating units of one of the claimed imidazole groups, or pyridine groups, or aniline groups.

### *Claim Rejections - 35 USC § 102*

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by US 5,698,531.

US 5,698,531 taught (see especially the abstract and columns 4-7) a process for delivering a polynucleotide complexed with a polymer into an extravascular parenchymal cell of a mammal by mixing the polynucleotide and the polymer to form a complex, wherein the zeta potential of the complex is less negative than that of the polynucleotide alone at physiological pH. The complex is delivered into a mammalian vessel *in vivo*, the permeability of the vessel is increased by increasing the pressure in the vessel, the complex passes through the vessel into the extravascular parenchymal cells and the polynucleotide is expressed.

### *Claim Rejections - 35 USC § 103*

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,698,531 in view of US 2001/0005717 A1.

The claims are drawn to a process for delivering a polynucleotide complexed with a polymer into an extravascular parenchymal cell of a mammal by mixing the polynucleotide and the polymer to form a complex, wherein the zeta potential of the complex is less negative than that of the polynucleotide alone at physiological pH. The complex is delivered into a mammalian vessel *in vivo*, the permeability of the vessel is increased by increasing the pressure in the vessel, the complex passes through the vessel into the extravascular parenchymal cells and the polynucleotide is expressed. The polymer may have at least one functional group with a pKa in the range of 5-7 and may consist of imidazole, or pyridine or aniline groups.

US 5,698,531 taught the invention as described above in the rejection under 35 USC 102.

US 5,698,531 did not teach that the polymer may have at least one functional group with a pKa in the range of 5-7 and may consist of imidazole, or pyridine or aniline groups.

US 2001/0005717 A1 taught (see especially paragraphs 49-55, example 13 and figure 14) a process of delivering a polynucleotide complexed with a polymer which has functional groups with a pKa in the range of 5-7 consisting of imidazole groups and transfecting the polynucleotide through a vessel into the surrounding tissues (parenchyma) of the vessel where the permeability of the vessel has been increased.

It would have been obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of US 5,698,531 with US 2001/0005717 A1 because

each of US 5,698,531 and US 2001/0005717 A1 teaches the use of a polymer complexed with a polynucleotide in a method of transfecting the polynucleotide through a vessel into the surrounding tissues (parenchyma) of the vessel where the permeability of the vessel has been increased. US 2001/0005717 A1 teaches the use of a polymer which has functional groups with a pKa in the range of 5-7 consisting of imidazole groups to increase the efficiency of the transfection.

One of ordinary skill in the art would have been motivated to combine the teachings of US 5,698,531 with US 2001/0005717 A1 because US 5,698,531 teaches the desirable and beneficial introduction of the polynucleotide complex into a vessel by increasing the permeability of the vessel and US 2001/0005717 A1 teaches the desirable and beneficial introduction of the polynucleotide complex into a vessel by increasing the permeability of the vessel where the polymer has functional groups with a pKa in the range of 5-7 consisting of imidazole groups for the additional benefit of increasing the efficiency of the transfection. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of US 5,698,531 and US 2001/0005717 A1.

### *Conclusion*

12. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or

applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Zeta Adams, whose telephone number is (703) 305-3291.

William Sandals, Ph.D.
Examiner
July 25, 2002

TERRY MCKELVEY
PRIMARY EXAMINER